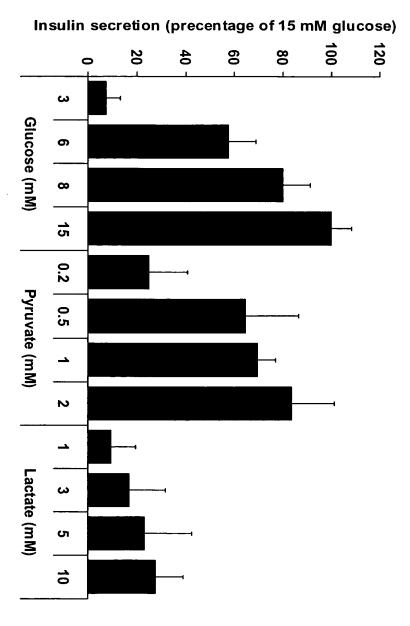


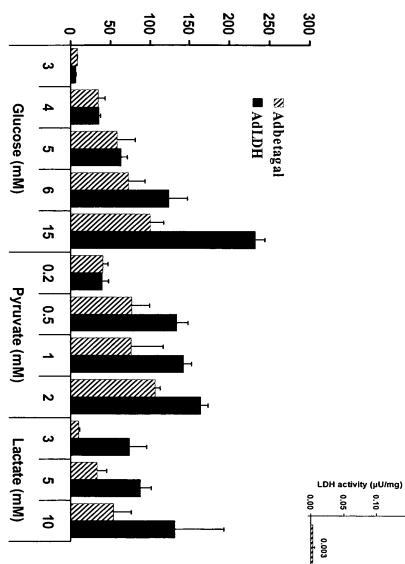
Fig. 1

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SSVPVWSGVNVAGVSLKSLNPQLGTDADKEQWKDVHKQVVDSAYEVIKLKGYTSWAIGLSVADLA QHGSLFLKTPKIVSSKDYSVTANSKLVIITAGARQQEGESRLNLVQRNVNIFKFIIPNVVKYSPQ MAALKDQLIVNLLKEEQVPQNKITVVGVGAVGMACAISILMKDLADELALVDVIEDKLKGEMMDL ESIMKNLRRVHPISTMIKGLYGIKEDVFLSVPCILGQNGISDVVKVTLTPDEEARLKKSADTLWG CKLLIVSNPVDILTYVAWKISGFPKNRVIGSGCNLDSARFRYLMGERLGVHPLSCHGWVLGEHGD IQKELQF









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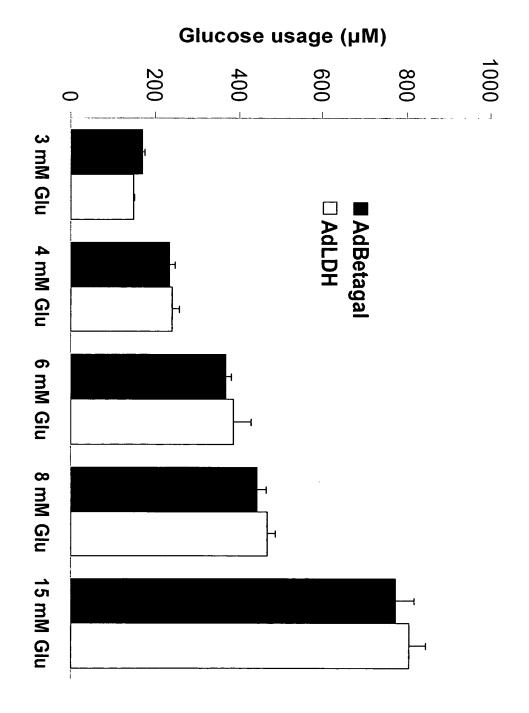
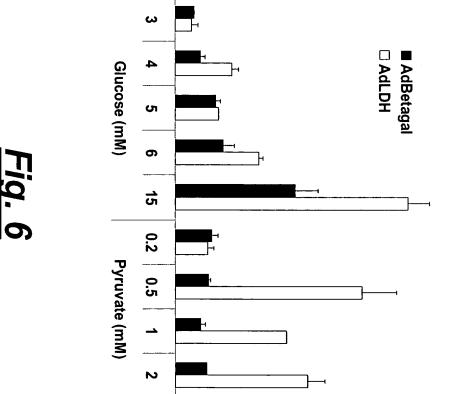


Fig. 5



100 -

Lactate output

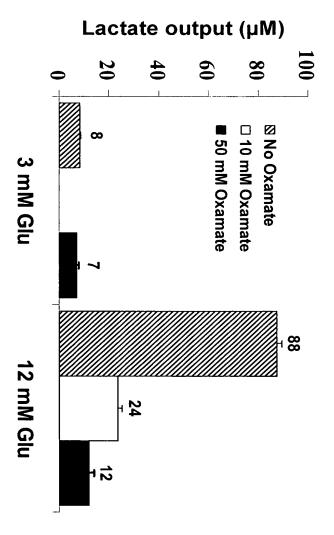
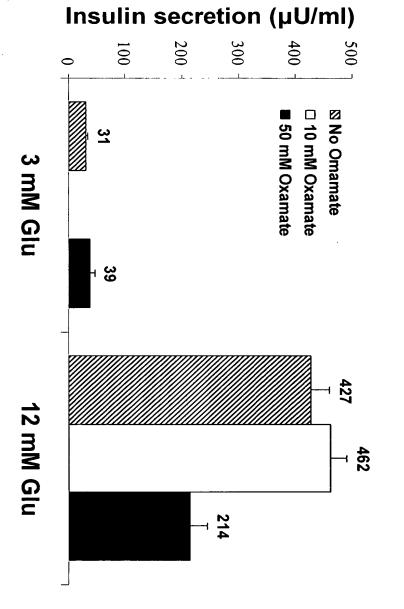


Fig. 7A

Insulin secretion



⁻ig. 7B

Pyruvate Cycling

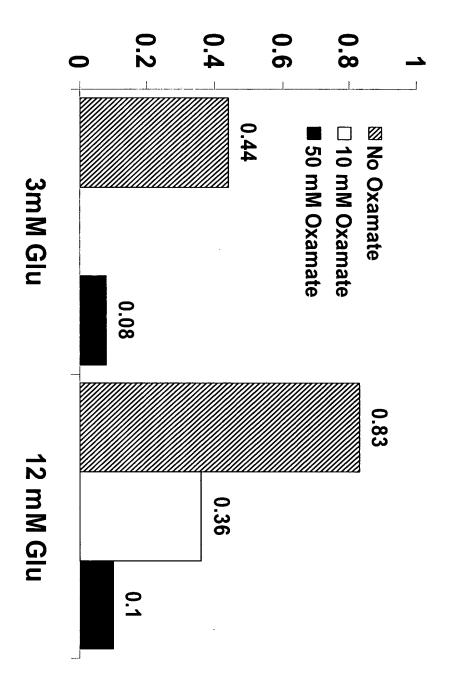


Fig. 7C

Oxamate inhibits Insulin secretion in islets

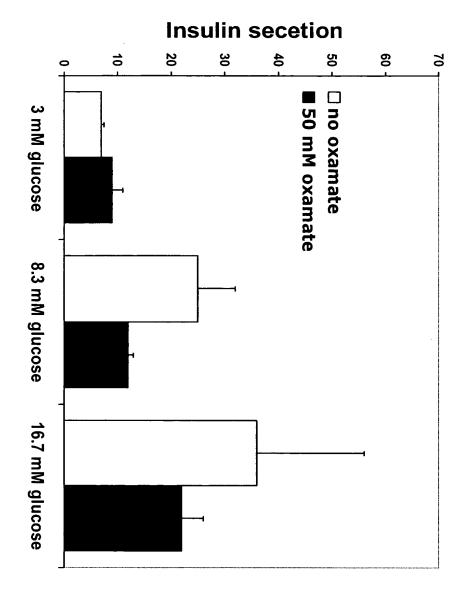
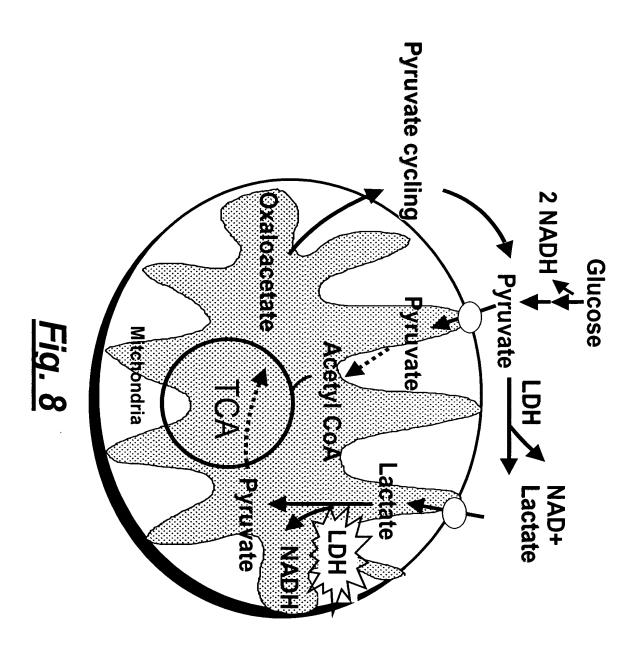
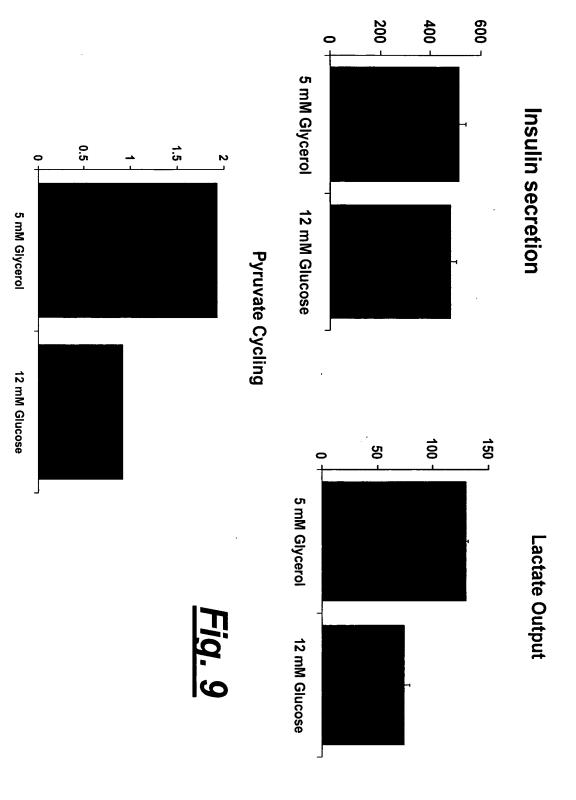


Fig. 7D



Production in Glycerol Kinase Expressing Cells. Pyruvate Cycling Correlates with Lactate



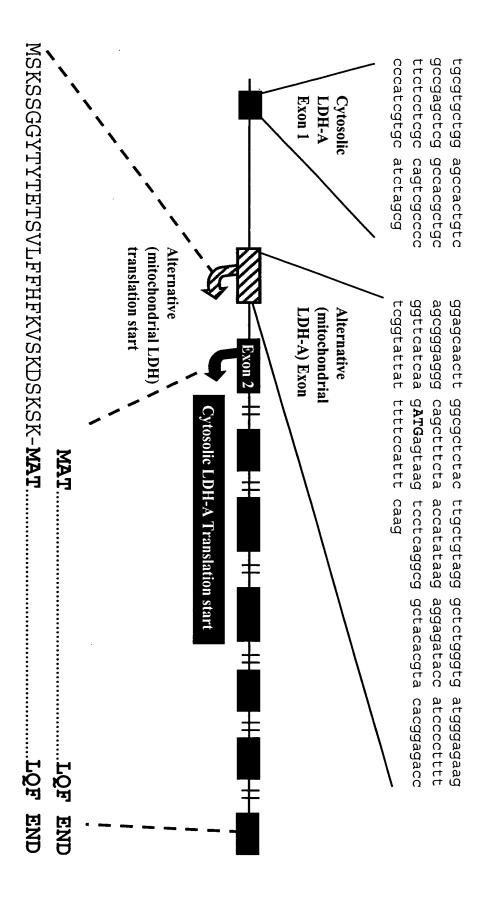


Fig. 10

among different species The N-terminal leader sequence is conserved

- Rat **MSKNSGGYTYTETSVLFFHFKVPKDSKSK**
- Mouse MSKSSGGYTYTETSVLFFHFKVSKDSKSK
- Human MGEPSGGYTYTQTSIFLFHAKIPFGSKSN
- MSK SGGYTYTETSVLFFHFKVPKDSKSK

CCCTTTTGGG GTTCATCAAG ATGAGTAAGA ACTCAGGCGG CTACACATAT ACGGAGACCT CAGTATTATT TTTCCATTTC

AAGGTCCCAA AAGATTCAAA GTCCAAG**ATG** GCAGCCCTCA AGGACCAGCT GATTGTGAAT CTTCTTAAGG AAGAACAGGT

CCTAGCACTT CACTGTCCAG GCTGCAGCAG GGTTTCTATG GAGACCACGC ACTTCTCATC TGA GCTGTGG TTAGTCCAGT GAGGAGGCCC AGGATGTCTT AAGCAGGTGG GGGAGTTCAT GGCTTCCCCA TGAAATACAG CCGTCAGCAA CTTAAGACAC CTTGGCCGAG ACGTCGCCGG CTGATGAGCT CCCCCAGAAC GCCTGAAGAA CCTCAGCGTC AGCATAATGA CCACTGAGCT AAAACAAAGT GAGGGAGAGA AAGATTACAG TTGACAGTGC CGTCTCCCTG CAAAAATTGT TGCCCTTGTT TCCACAGTGC GAGTGCAGAT CCATGTATCC AGAACCTTAG ATACGAAGTG CTCCAGCAAA GATGTCATAG GTCACGGGTG TATTGGAAGT AAACTGCTCA GCCGGCTCAA TIGTIGGGGI AAGTCTCTGA ACCCTCTGGG TGGGACAAAA GCGGGTGCAT ATCAAGCTGA GGTCCTGGGA GGTTGCAATC TCGTCTCAAA GATTATAGTG AAGATAAGCT TGGTGCTGTT ACCCGCAGCT TTTGGTCCAG TGGAATCTCA GAATCCAGAA CCCATTTCCA AAGGTTACAC GGGCACGGAT GAGCATGGCG TGGATTCGGC CCCAGTGGAT CGAAACGTGA AAAGGGAGAG GGCATGGCTT TGACTGCAAA GGAGCTGCA G GTGCCATCA G GATGTTGTG A CCATGATTA A ATCCTGGGC C GCAGACAAG G ACTCCAGTG T TCGGTTCCG T ATCTTGACC T ACATCTTCA A CTCCAAGCT G ATGATGGAT C TTCTAAAGTC GGGTCTCTAT AGGTGACACT GCCTGTGTGG GTTCATCATT ATTGGCCTCT AGCAGTGGAA TACCTGATGG ACGTGGCTTG GTCATTATCA TTCAGCATGG TATCTTAATG GACTCCTGAC GGGATCAAGG CCGTGGCAGA AGTGGTGTGA GAGAAAGGCT CAGCCTTTTC AAGGACTTGG GGATGTGCAC GAAGATCAGC CCAAATGTTG cceceeeec TTCCCAGTGI

- * Mitochondrial start site
- \$ cytosolic start site
- Overlined 5'ORF
- Primer sequences are underlined

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SARFRYLMGERLGVHALSCHGWVLGEHGDSSVPVWSGVNVAGVSLKSLNPELGTDADKEQWKEVH MSKSSGGYTYTETSVLFFHFKVSKDSKSKMATLKDQLIVNLLKEEQAPQNKITVVGVGAVGMACA QNGISDVVKVTLTPEEEARLKKSADTLWGIQKELQF KQVVDSAYEVIKLKGYTSWAIGLSVADLAESIMKNLRRVHPISTMIKGLYGINEDVFLSVPCILG EGESRLNLVQRNVNIFKFIIPNIVKYSPHCKLLIVSNPVDILTYVAWKISGFPKNRVIGSGCNLD ISILMKDLADELALVDVMEDKLKGEMMDLQHGSLFLKTPKIVSSKDYCVTANSKLVIITAGARQQ

CCCAATAAACCTTGAACAGTG AGTGAGTCACATCCTGGGATCCAGTGTATAAATCCAATATCATGTCTTGTGCATAATTCTTCCA AAGGATCTTATTTTGTGAACTAT TGCCCCTTGAGCCAGGTGGATGTTTACCGTGTGTTATATAACTTCCTGGCTCCTTCACTGAACA TGCCTAGTCCAACATTTTTTCCC ATTAATCTTGTGTAGTCTTCAACTGGTTAGTGTGAAATAGTTCTGCCACCTCTGACGCACCACT GCCAATGCTGTACGTACTGCATT TCACTGTCTAGGCTACAACAGGATTCTAGGTGGAGGTTGTGCATGTTGTCCTTTTTATCTGATC TGTGATTAAAGCAGTAATATTTT TCTCTGTAGCAGATTTGGCAGAGAGTATAATGAAGAATCTTAGGCGGGTGCACCCAGTTTCCAC CATGATTAAGGGTCTTTACGGAA CCAGTGTGCCTGTATGGAGTGGAATGAATGTTGCTGGTGTCTCTCTGAAGACTCTGCACCCAGA TTTAGGGACTGATAAAGATAAGG ATCCAGTGGATATCTTGACCTACGTGGCTTGGAAGATAAGTGGTTTTCCCCAAAAACCGTGTTAT TGGAAGTGGTTGCAATCTGGATT AAGATGGACTGGGAAAAACATCAACTCCTGAAGTTAGAAATAAGAATGGTTTGTAAAATCCACA GCTATATCCTGATGCTGGATGGT AAGAGGCCCGTTTGAAGAAGAGTGCAGATACACTTTGGGGGATCCAAAAGGAGCTGCAATTTTA AAGTCTTCTGATGTCATATCATT AACAGTGGAAAGAGGTTCACAAGCAGGTGGTTGAGAGTGCTTATGAGGTGATCAAACTCAAAGG CTACACATCCTGGGCTATTGGAC $\tt CAGCCCGATTCCGTTACCTGATGGGGGAAAGGCTGGGAGTTCACCCATTAAGCTGTCATGGGTG~GGTCCTTGGGGAACATGGAGATT$ TGGTCCAGCGTAACGTGAACATATTTAAATTCATCATTCCTAATGTTGTAAAATACAGCCCGAA CTGCAAGTTGCTTATTGTTTCAA GCAAAGACTATAATGTAACTGCAAACTCCAAGCTGGTCATTATCACGGCTGGGGCACGTCAGCA AGAGGGAGAAAGCCGTCTTAATT AGATTACAGTTGTTGGGGTTGGTGCTGTTGGCATGGCCTGTGCCATCAGTATCTTAATGAAGGA CTTGGCAGATGAACTTGCTCTTG TTGATGTCATCGAAGACAAATTGAAGGGAGAGATGATGGATCTCCAACATGGCAGCCTTTTCCT TAGAACACCAAAGATTGTCTCTG TTCCTTTTGGTTCCAAGTCCAATATGGCAACTCTAAAGGATCAGCTGATTTATAATCTTCTAAA GGAAGAACAGACCCCCCAGAATA ${\tt CCCCACTTGGTTAATAAACCGCGATGGGTGAACCCTCAGGAGGCTATACTTACACCCAAACGTC}$ GATATTCCTTTTCCACGCTAAGpCTCTGGTGTTTACTTGAGAAGCCCTGGCTGTGTCCTTGCTGGTAGGAGCCGGAGTAGCTCAGAGT GATCTTGTCTGAGGAAAGGCCAC

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ClustalW (vl.4) multiple sequence alignment

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285 285 275	DTDDTTDDDTTDTTDADATTADAADAADAADADAADAADA	236	ratmitLDHcloned humanmitLDHmRNA mousemitLDHmRNA	
235 235 225	TOTTOTAADTO-TTADTODAOOAGGAACTOOOBGAGAACTOTOAACACTOTOTAA-TATTTADTODAOTADDAAATOTOAACDGTAAACCTDAACCTAACCTAACCTAACCTAACCTAA	781 781	ratmitLDHcloned humanmitLDHmRNA mousemitLDHmRNA	
98T 98T 9LT	TTABAAAADDDTBAADTTTTADTTTTTATAADTDDAABABDATATA TTABATTTTDTTABAATDBAATD	LET	ratmitLDHcloned humanmitLDHmRNA mousemitLDHmRNA	
136 136 156	DADATOBOOBGADTOAABAATBABTABAADTADTTDBBTTT-TOODT DATATOBBABBACTCOOAABTBBBTABCOCOCAAATAATTBTTCACOCOCO DADATOBBOBBACTCOTBAATBABTABAACTACTT-BBTTTT-COCOT ** ***** ****** * * * * * * * * * * *	48	ratmitLDHcloned humanmitLDHmRNA mousemitLDHmRNA	
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832	DADAADTOTOTOTOTOTOTTAADTAADTAADTATOTOTOTO	984	humanmitLDHmRNA
878	CTDAADTCCTCTCDCDCCCCTCTAADTCTCAADTCTCTCTC	9 <i>LL</i>	ratmitLDHcloned
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587	TTCACGCGCTGAGCTGTCACGGCTGGGTCCTGGGGAGAGAGA		MOUSEmitLDHmRNA
287	TTCACCCATTAAGCTGTCATGGGTGGTGGTGGTGGTGGTGTTCC		humanmitLDHmRNA
SLL	COLORDO DE LA COL	927	ratmitLDHcloned
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257	DEPOSITION OF THE PROPERTY OF T		AMAmHGJjiməavom
732	DADDDTODDAAADDDDDTADTOOATTDOOTTADOOODAOTTADDTOTAAO		AMAmHQJjimnsmud
725	CAATCTGGATTCGGCTCGGTTACCTGATGGGAGAAAGGCTGGGAG	949	ratmitLDHcloned

982	DTTDDTDAADDTTAATDADDDAAAAADDCTTTDDDTDADTAAAADDTTDD	989	MOUSEMİtLDHmRNA
982	DTTDDTDAADDTTATTDTDDDAAAAADDCTTTTDDTDAATADAADDTTDD	989	humanmitLDHmRNA
S L 9	GCTTGGAAGATCAGCGCTTCCCCAAAACAAAGTTATTGGAAGTGGTTG	979	ratmitLDHcloned
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932	DTDCATTCTATADDTDACCTAACTTTTTATTCTTTDAACDTCA	985	ANAmHUJʻimnamud
929	AGTGCAAACTGCTCATCGTCAACCCAGTGGATTTTTTTTT	945	ratmitLDHcloned
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282	ADOCOCATATATATATATATATATATATATATATATATATAT	989	AUAmHGJJimaannd
SLS	DADDIDADATAAADTTTTAAADDTTADTADTADAATACAGTCCAC	226	ratmitLDHcloned
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232	AATƏDƏADOTDƏTTTAATTOTƏDDƏAAAƏAƏƏƏAƏAADƏAOTƏDAƏ	98₺	humanmitLDHmRNA
225	AAADOBACCETCAACTAGACGACAAAAAAAAAAAAAAAAAAAAAAA	9∠₹	ratmitLDHcloned
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45 E	ASSTSTEAMAAASSASAATTSSTTTTSSBASBTASBASTTSTABB	975	ratmitLDHcloned
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382	TADTADADDDAADTTAAADADAADDTADTTTTTTTTTTT	336	humanmitLDHmRNA
SLE	TADTADADDDAAATDDAATADAADATADTADTTDTTDCCCTTGTADTAD	326	ratmitLDHcloned

Fig. 13B

Fig. 13C

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RIET	TOTAD-AAADDDDTDTDDTADADTTDTD-D-TDADATDATTDDTDTD	97.ZT	моиземісьынткия
	TOAADTADAAAAAAAAACGACTGGGAAAAACTTATATATATATATATA		•
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1290	DAAADDTD-DTTDADTDTDTD	5961	ratmitLDHcloned
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1274	6A9TOT9OT-OTT-OOOAOAOOAOBAO99ATOTTO999AO9AO	1235	ANAmHddtimeauom
1281	CAACAGGATT-CTAGGTGG-AGGTTGTGCATGTTGTCTCTGAT	1234	humanmitlDHmRNA
₹ 97T	CAGCAGGGTTTCTATGG-AGACCACGCAC-TTC-TCATCTGAG	ISS2	xstmitLDHcloned
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₹52T	CTGCAGTTCTAAAGTCTTCCCCGTGTCTAACATCTTCACTGTCACGCTG	SRTT	моиземістримкия
	ATOGORATTTACACTCTTCT-GATGTCATATCACTTTCACGTCTACGGCTA		•
	6TOBBACOTTCTACTTCACDATCOTTCTAAATCTTGACOTTCACATCTGACATCTACATCAT		•
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	AGGCCCGCAAGAAGAAGACGCAACACCCTCTGGGGAAACACGAAGAAGAAGAAGAAGAAGAAGAAGAAGAA		-
	DABBAAADCTABBBBBTTTCACATABACBTAABAABAABTTTCCCAAAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAA		
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113 4	DAADDADTCTCTGGBTGTTGTADAGCTGACACTGACTGACTGACTGACGGAAG	580T	MOUSEMITLDHMRNA
113 1	ACAGAATCTCAGACCTTGTGAAGGTGACTCTGAGGAAG	SBOT	humanmitlDHmRNA
	ACAAAATCTCAGATGTTGTGAAGGTGACACTGACTCCTGACGAGG		
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₽80I	CTCTATGGAATCAATGAGGATGTCTTCCTCAGTGTCCATGTAAGGTATCTGGG	SEOT	тоизеттельныкия
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	CTCTATGGGATCAAGGAGGATGTCTTCCTCAGCGTCCATGTAGGGGGGGG		
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	T999AATTA9TACCACCTTT-ACCCTTACGGGGGGGGGGGGGGGGGGGGG		MNAmHGLJimeanom
	T999AATTA9TACCACCTTPACCC-ACCTGGATTATATATATATATATATATATATATATATATA		ANAmHddjimasmud
1024	T999AATTA9TACCATCTT-ACCCTGCGGGGGGGGTGACATTAAGAAATTAA	916	ratmitLDHcloned
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586	TATSASASSTTTASASSATSTSTSASSTTATSSSSTSSTASASAT	986	ANAmHddtimnsmud
SL6	TACSASASOCOTTCASACSSTACTCCTCCCTCACACCTTCACACACCTTCA	976	ratmitLDHcloned
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586	TDBAAADTDBAADTADTDBADGTGATGATGATGATGATGATGATGATGATGATGATGATGA	988	ANAmHGLItmeway
386	$\verb"DD2AAACTAATTADADATATTCDADADATTDD2ADAACTT"$	988	humanmitLDHmRNA
928	${\tt TGCACACTCAACTACTACTACTACTACTACTACTACTACTAC$	948	ratmitLDHcloned
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882	TCTTAACCCAGAACTGGGCACTGACGAGACAAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGA	988	MousemitLDHmRNA
S88	TCTGCACCCAGATTTAGGGACTGATAAAGATAAGGAACAGTGGAAAGAGG	988	АИЯшНСТЭтшавти
S & 8	TTABAACCCGCAGCTGGGCACGAGACACAGAGGAGCAGTGGAACGTG		ratmitLDHcloned

	0891	DTDADAAATTDDAAAATAAADDDTADT		
		DT9ADAAATTDDA-AATAADDDDAAAATDAADDATATT		•
	1290		1521	ratmitLDHcloned
		DAADDAADDTADATADDTDTADAATDTADADTDTA		· · · · · · · · · · · · · · · · · · ·
1723 1733	ĐTĐAADDTAT:	DAADDAADBTAADAAADATADATDTABAAA-AATĐTA		
1661			1661	ratmitLDHcloned
		ADDIDITALITATATATATATATATATATATATATATATATATAT		•
	ATATADDATTA	ADATOTATATATOAGATOTTATTATTOAGAACA		
1290			1621	ratmitLDHcloned
		OSTETICITATACETACCATACATATACACC		· · · · · · · · · · · · · · · · · · ·
	DTTDTTAATA	CTGGGATCCAGTGTAAATCCAATAT-CATGTCTTGTGC		
1590			1621	ratmitLDHcloned
		4TT9ADDDTT9AĐDAĐDDĐATDDĐ-ADAAADDADĐTD		
52ST 06ZT	-DTADADTDA	O-T9ACOCTGAACATGCCAACATTTTTTTTCCAGT-0		
36 C L			1661	ratmitLDHcloned
		CCCCTG-TG-A-GCC-TGCTGC-A-		•
TEST D6ZT	STSSSTSSTT	DAATATATTƏTƏDƏSATTTƏTAƏƏTƏƏAƏDƏAƏTƏTƏ		ratmitLDHcloned humanmitLDHmRNA
3621			1661	bego[pWG.14;mtex
		- D-ADDTDAADDDTDA-DADADTDTDTDTDADDDTD		•
189T	9TTTAD9TDA1	TECH TOTAL STATE TO THE TECH T		ratmitLDHcloned humanmitLDHmRNA
3661			1961	bego[pHG.14 imtex
		TTGCAACTGCATATCTGTGTGTGTGACCTGTTA		
	ATAAADTDTD/	TGCTGGATGTAATCTTGTGTAGTCTTCAACTGGTTA		•
1590			1521	ratmitLDHcloned
		D6A9A999A		
	ASTOCTATATO	DEADADOTAAAATUTTGETAABAATAABATTDAABC		
759C			1621	ratmitLDHcloned

1680

Fig. 14